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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/713,970	11/14/2003	Roland Contreras	17106	5158

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EXAMINER	
GEBREYESUS, KAGNEW H	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 05/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/713,970	CONTRERAS ET AL.	
	Examiner	Art Unit	
	Kagnew H. Gebreyesus	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-38* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-27 are drawn to a genetically engineered methylotropic yeast strain transformed with a nucleotide sequence coding for a glycoprotein to produces a glycoprotein having a mammalian-like N-glycan structure modified to expresses (1) an α-1, 2-mannosidase or a functional part thereof, (2) an N-acetyl-glucosaminyltransferase I (or GnTI) or a functional part thereof, and (3) a β-l,4-galactosyltransferase (Ga1T) or a functional part thereof, and wherein the genomic OCHI gene in the modified strain is inactivated classified in class 435, subclass 254.11.

II. Claims 28, 29, 31 and 32 are drawn to a method of recombinantly producing a glycoprotein having a mammalian-like N-glycan structure in a methylotrophic yeast strain, comprising transforming said strain with a nucleotide sequence coding for said glycoprotein; modifying said strain such that the modified strain expresses (1) an α-1,2-mannosidase or a functional part thereof, (2) an N-acetylglucosaminyltransferase I (or GnTI) or a functional part thereof, and (3) a β-l,4-galactosyltransferase (Ga1T) or a functional part thereof, and wherein the

genomic OCHI gene in the modified strain is inactivated; and producing said glycoprotein in the modified stain. classified in class 435, subclass 69.1.

III. Claims 30 and 33 are drawn to a glycoprotein produced in a methylotrophic yeast strain having a mammalian-like N-glycan structure, classified in class 530, subclass 395.

IV. Claim 34 is drawn to vector comprising a nucleotide sequence coding a GalT, operably linked to a promoter sequence and a 3' termination sequence, wherein said promoter sequence and said 3' termination sequence are functional in a methylotrophic yeast stain to achieve expression of said GalT in said stain classified in class, 435, subclass 320.1

V. Claims 35 and 38 are drawn to a kit comprising (1) a vector comprising a nucleotide sequence coding for an α-1,2-mannosidase or a functional part thereof, (2) a vector comprising an N-acetylglucosaminyltransferase I (or GnTI) or a functional part thereof, and (3) a vector comprising a β-l,4-galactosyltransferase (GalT) or a functional part thereof wherein each of the vectors is capable of directing the expression of the encoded protein further comprising a gene capable of disrupting the genomic OCHI gene further comprising a vector encoding a glycoprotein heterologous to said methylotrophic strain in a methylotrophic strain and the methylotrophic strain classified in class 435, subclass 6.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions in groups I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the methylotrophic yeast can be used to produce the various enzymes instead of the glycoprotein.

3. Inventions in groups II and III are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make another and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant the glycoprotein can be chemically synthesized. In addition the method of invention II can be used to produce other products such as the three enzymes (α-1, 2-mannosidase, the N-acetylglucosaminyltransferase I (or GnTI) and the β-l,4-galactosyltransferase (GalT)).

4. Inventions in groups I and III are independent. The methylotrophic yeast strains and the glycoprotein each comprise unrelated structure capable of separate manufacture, use and effect. Inventions are unrelated if it can be shown that they are not disclosed as being capable of use together and they have different modes of operation, different function, or different effects (MPEP 806.04, MPEP 808.01). In the instant case the methylotrophic yeast strains are separate and distinct from the glycoproteins in invention III as they are physically and functionally distinct entities.

5. Inventions in group III are unrelated to inventions in group IV. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, invention of IV is drawn to a vector comprising a single gene encoding a GalT which is insufficient to produce the glycoprotein of III and invention III is drawn to a glycoprotein.

6. Inventions in group I are unrelated to inventions in group IV. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, invention of IV is drawn to a vector comprising a single gene encoding a GalT which is unrelated to the genetically engineered methylotrophic yeast strain transformed with various constructs to produce the glycoprotein having a mammalian-like N-glycan structure.

7. Inventions V and IV are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination (V) as claimed does not require the particulars of the subcombination as claimed because the vector in the kit does not necessarily require the promoter and terminator. The subcombination has separate utility such as the use of the vector comprising the GalT to produce the GalT enzyme.

8. Inventions I and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the inventions of V can be used to

make the invention in I however the invention in I and V cannot be used together and are mutually exclusive.

9. Inventions III and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the glycoprotein of invention III comprises a mammalian-like N-glycan structure which is not comprised in the kit.

10. Inventions in group II and invention in group V are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the kits of invention V can be used to produce the three enzymes (α-1, 2-mannosidase, the N-acetylglucosaminyltransferase I (or GnTI) and the β-l,4-galactosyltransferase (Ga1T)) which in turn can be used to produce the antibodies.

In addition the search and examination of each method in Groups I-V in one patent application would result in undue burden, since the searches for all the groups are not co-extensive, since the searches are in different classifications, and involve different field of search. Each of the of the inventions requires a separate patent and non-patent literature search requiring a different text search for each group and thus co examination of the inventions in groups I-V would be a serious burden on the examiner.

In addition if applicants elect the invention in group I, they must also elect the specific origin of the methylotrophic yeast strain from the following group:

(a) Candida, (b) Hansunella, (c) Torulopsis or (d) Pichia

Furthermore, applicants must elect the origin of the enzymes ((1) α-1, 2-mannosidase, (2) N-acetylglucosaminyltransferase I (or GnTI) and (3) the β-l, 4-galactosyltransferase (Gal1T) to be expressed in the methylotrophic strain from the following species:

(i) Human (ii) rabbit (iii) rat, (iv) plant (v) insect, (vi) nematode

(vii) protozoa (viii) Aspergillus (ix) Trichoderma reesei.

This species are distinct because the glycosylation machinery in each of the straines is different. In addition the specific enzymes (α-1, 2-mannosidase, N-acetylglucosaminyltransferase I (or GnTI) and β-l, 4-galactosyltransferase (Gal1T)) from various origins have different polynucleotide sequences and thus have patentably distinct structures.

1. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

2. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.43).

3. Applicant is reminded that upon the cancellation of claims to a none elected invention the none elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48 (b) and by the fee required under 37 CFR 1.17 (i).

4. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

5. In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double

patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kagnew H Gebreyesus whose telephone number is 571-272-2937. The examiner can normally be reached on 8:30am-5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Achutamurthy ponnathapura can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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